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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,816	09/01/2006	Makoto Asashima	P28509	1458

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GREENBLUM & BERNSTEIN, P.L.C.
1950 ROLAND CLARKE PLACE
RESTON, VA 20191

EXAMINER	
ARIANI, KADE	

ART UNIT	PAPER NUMBER
1651	

NOTIFICATION DATE	DELIVERY MODE
02/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary	Application No.	Applicant(s)	
	10/549,816	ASASHIMA ET AL.	
	Examiner	Art Unit	
	KADE ARIANI	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7 and 8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7 and 8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/25/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed on November 13, 2008, has been received and entered.

Claims 4-6 and 916 have been canceled.

Claims 1-3, 7 and 8 are pending in this application and were examined on their merits.

Claim Objection

Objection of Claims 1, 4, 5, 6, and 10-16 is withdrawn due to Applicant's amendments to the claims filed on 11/13/2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection under 35 U.S.C. 112, first paragraph, is withdrawn due to Applicant's amendments to the claims filed on 11/13/2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of Claim 7 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is withdrawn due to Applicant's amendments to the claims filed on 11/13/2008.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102(b) as being anticipated by Drysdale et al. (Developmental Biology, 1997, Vol. 188, p.205-215).

Claims 1 and 2 are drawn to a method for forming autonomically beating cardiac muscle-like cell aggregates from stem cells derived from a vertebrate animal *in vitro* which comprises the step of culturing the stem cells derived from a vertebrate animal in

the presence of a retinoic acid X receptor (RXR) ligand, and wherein the RXR ligand is a RXR agonist or antagonist.

Drysdale et al. disclose a method for forming autonomically beating cardiac muscle-like cell aggregates from stem cells derived from a vertebrate animal *in vitro,* comprises the step of culturing the stem cells derived from a vertebrate animal in the presence of a retinoic acid X receptor (RXR) ligand (treatment of heart region explants taken from normal embryos with retinoic acid (RA) and control explants differentiate to form cardiac tissue (p.212 Figure 5. Legend).

Drysdale et al. therefore clearly anticipate the claimed method.

Claim 7 is rejected under 35 U.S.C. 102(b) as being anticipated by Moriya et al. (Develop. Growth Differ. , 2000, Vol. 42, p.593-602).

Claim 7 is drawn to a method for forming a tissue having morphology and function of a pancreas from stem cells derived from a vertebrate animal *in vitro* which comprises culturing the stem cells derived from a vertebrate animal in the presence of a retinoic acid receptor ligand together with activin wherein said retinoic receptor ligand does not substantially bind to the retinoic receptor subtype γ.

Moriya et al. disclose a method for *in vitro* pancreas formation from *Xenopus* ectoderm isolated from embryos (stem cells derived from a vertebrate animal), culturing stem cells derived from a vertebrate animal in the presence of all-trans- retinoic acid (please note that all-trans-retinoic acid is a RXR subtype-α ligand) and activin (see Abstract and p.594, 1st column 2nd and 3rd paragraphs).

Moriya et al. therefore clearly anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moriya et al. (Develop. Growth Differ. , 2000, Vol. 42, p.593-602) in view of Takahashi et al. (Journal of Medicinal Chemistry, August 2002, Vol. 45, No. 16, p.3327-3330).

Claims 7 and 8 are drawn to a method for forming a tissue having morphology and function of a pancreas from stem cells derived from a vertebrate animal *in vitro* which comprises culturing the stem cells derived from a vertebrate animal in the presence of a retinoic acid receptor ligand together with activin wherein said retinoic receptor ligand does not substantially bind to the retinoic receptor subtype γ, and wherein the RAR ligand is 4-[(5, 6, 7, 8,-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl] benzoic acid.

As mentioned immediately above, Moriya et al. teach the limitations of claim 7.

Moriya et al. do not teach the RAR ligand is 4-[(5, 6, 7, 8,-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl] benzoic acid. However, Takahashi et al. teach

retinoic acid receptor (RAR) agonist 4-[(5, 6, 7, 8,-tetrahydro-5,5,8,8-tetramethyl-2-naphthalenyl)carbamoyl] benzoic acid (Am80). (Abstract, Introduction 1st column, p.3328 2nd column lines 1-2, p.3328 Chart 1.).

Therefore, in view of the above teachings, a person of ordinary skill in the art at the time the invention was made could have been motivated to use the retinoic acid receptor ligand as taught by Takahashi et al. in the method as taught by Moriya et al. with predictable results of regulating the activity of the retinoic acid receptor. The motivation as taught by Takahashi et al. would be to devise new therapeutic strategies against the incurable disease diabetes.

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Drysdale et al. (Developmental Biology, 1997, Vol. 188, p.205-215) in view of Takahashi et al. (Journal of Medicinal Chemistry, August 2002, Vol. 45, No. 16, p.3327-3330).

Claims 1-3 are drawn to a method for forming autonomically beating cardiac muscle-like cell aggregates from stem cells derived from a vertebrate animal *in vitro* which comprises the step of culturing the stem cells derived from a vertebrate animal in the presence of a retinoic acid X receptor (RXR) ligand, wherein the RXR ligand is a RXR agonist or antagonist, and retinoic acid X receptor ligand is 2-[N-cyclopropyl-methyl-N-(5, 6, 7, 8-tetrahydro-5, 5, 8, 8-tetramethynaphtahlene-2-yl)amino]pyrimidin-5-carboxylic acid.

As mentioned immediately above, Drysdale et al. teach the limitations of claims 1 and 2. Drysdale et al. also teach heart development is sensitive to retinoic acid and

myocardial differentiation pathway is sensitive to RA signaling (Abstract and p.206 1st column 2nd and 3rd paragraphs).

Drysdale et al. do not teach RXR agonist is PA024 or 2-[N-cyclopropyl-methyl-N-(5, 6, 7, 8-tetrahydro-5, 5, 8, 8-tetramethynaphtahlene-2-yl)amino]pyrimidin-5-carboxylic acid). However, RXR agonist is PA024 or 2-[N-cyclopropyl-methyl-N-(5, 6, 7, 8-tetrahydro-5, 5, 8, 8-tetramethynaphtahlene-2-yl)amino]pyrimidin-5-carboxylic acid (Abstract. p.3328 Chart 1., p.3329 1st column 2nd paragraph, lines 10-17).

Therefore, a person of ordinary skill in the art at the time the invention was made could have been motivated to use the retinoic acid receptor ligand as taught by Takahashi et al. in the method as taught by Drysdale et al. with predictable results of regulating the retinoic acid receptor function. The motivation as taught by Drysdale et al. would be the role of retinoic acid receptor in heart development

Response to Arguments

Applicant's arguments filed on 11/13/2008 have been fully considered but they are not persuasive.

Applicant argues that Takahashi and Moriya fail to disclose stem cells. Applicant argues that the cells from which Moriya forms a pancreas are ectoderm and ectoderm cells are not stem cells, and human promyelocytic leukemia cells HL-60 are not stem cells.

However, specification page 6 last paragraph especially lines 5 and 7, disclose stem cells such as embryonic stem cells and embryoid bodies can be used. Medical dictionary online (11 March 2008) defines ectoderm, the outer layer of the three germ layers of the embryo. Thus, Moriya disclose stem cells.

Moreover, at the time the invention was made it was very well known in the art that human promyelocytic leukemia cells HL-60 are stem cells (see Abstract lines 13-16 of Fontana et al. , PNAS 1981, Vol. 78 No.6 p.3863-3866). Thus, Takahashi disclose stem cells.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kade Ariani
Examiner
Art Unit 1651

/Leon B Lankford/
Primary Examiner, Art Unit 1651